

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

Service Category

- | | |
|--|---|
| ☐ Anesthesia | ☐ Medicine Services and Procedures |
| ☐ Surgery | ☐ Evaluation and Management Services |
| ☐ Radiology Procedures | ☐ DME/Prosthetics or Supplies |
| ☐ Pathology and Laboratory Procedures | ☒ Part B Drug |

Service Description

This document addresses the use of intravitreal **vascular endothelial growth factor (VEGF) antagonists**. Overexpression of VEGF is thought to contribute to diabetic retinopathy, and other retinal disorders associated with neovascularization.

Agents addressed in this clinical guideline include:

- Avastin (bevacizumab) and biosimilars: Alymsys (bevacizumab-maly); Mvasi (bevacizumab-awwb); Vegzelma (bevacizumab-adcd); Zirabev (bevacizumab-bvzr)
- Beovu (Brolucizumab-dblI)
- Eylea (Aflibercept) and biosimilars: Yesafili (aflibercept-jbvf), Opuviz (aflibercept-yszy), Ahzantive (aflibercept-mrbb), Pavblu (aflibercept-ayyh), and Enzeevu (afilbercept-abzv)
- Lucentis (Ranibizumab) and biosimilars: Byooviz (ranibizumab-nuna); Cimerli (ranibizumab-cqrn)
- Vabysmo (Faricimab-svoa)
- Susvimo (Ranibizumab)

Background Information

Avastin (bevacizumab) is humanized anti-VEGF antibody which blocks all VEGF isoforms. Lucentis (ranibizumab) and its biosimilars Byooviz (ranibizumab-nuna) and Cimerli (ranibizumab-cqrn) are truncated forms of bevacizumab. Cimerli is designated by the FDA as an interchangeable product to Lucentis. Beovu (brolucizumab) is a humanized single-chain antibody fragment that blocks all VEGF-A isoforms. Eylea (aflibercept) is a recombinant fusion protein that binds to VEGF-A as well as Placental Growth Factor (PIGF). Macugen is an RNA aptamer that binds and neutralizes VEGF. Vabysmo (faricimab-svoa) is a humanized bispecific antibody that targets both VEGF-A and angiopoietin-2 (Ang-2).

Avastin is most often used intravenously as an anti-cancer agent. While it is not FDA approved to be used intravitreally or for any ocular conditions; it is widely used in ophthalmology. Compounding pharmacies often repackage Avastin into single-use units for use by ophthalmologists. FDA and the American Academy of Ophthalmology (AAO) have issued warnings regarding the importance of obtaining repackaged Avastin from compounding pharmacies accredited by National Boards of Pharmacy to avoid the potential for contaminated products.

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

- A. **Age-related macular degeneration (AMD):** AMD is an eye disease characterized by progressive degeneration of the macula and is the leading cause of vision loss in older adults. When AMD results in the development of abnormal blood vessels behind the retina, the condition is commonly referred to as “wet” or neovascular AMD. These new blood vessels tend to be fragile and loss of central vision can occur quickly over the course of weeks to months. Although most patients with advanced AMD do not become completely blind, significant visual loss can lead to disability. The AAO Preferred Practice Pattern (PPP) on AMD states, “Intravitreal injection therapy using anti-VEGF agents (e.g. aflibercept, bevacizumab, and ranibizumab) is the most effective way to manage neovascular AMD and represents the first line of treatment.” Beovu is also approved for the treatment of neovascular age-related macular degeneration and is recommended in the AAO PPP. However, post marketing safety reports and new warnings about retinal vasculitis and/or retinal vascular occlusion have prompted concerns around its relative safety profile. Although Macugen is FDA-approved for AMD, it does not improve visual acuity in patients with new-onset neovascular AMD and is rarely used in current clinical practice.
- B. **Retinal vein occlusion:** A blockage of the blood supply from the retina causes retinal vein occlusion. This condition most often affects older individuals and can be caused by a blood clot, diabetes, glaucoma, atherosclerosis or hypertension. Retinal vein occlusion is the second most common type of retinal vascular disease and is estimated to involve 180,000 eyes per year. The AAO PPP for retinal vein occlusion states, “Macular edema may complicate both central retinal vein occlusions (CRVOs) and branch retinal vein occlusions (BRVOs). The first line of treatment for the associated macular edema is anti-VEGFs.”
- C. **Diabetic retinopathy (DR) and diabetic macular edema (DME):** Diabetic retinopathy is one of the leading causes of blindness in working-age Americans. Approximately 28% of adults with diabetes over the age of 40 develop DR. DR and DME are caused by chronically high blood sugar which disrupts blood flow and causes damage to the tiny blood vessels in the retina. In its most advanced stage, DR can cause new abnormal blood vessels to grow on the surface of the retina, which can lead to scarring and visual disturbance. This severe form is called proliferative diabetic retinopathy (PDR). Sometimes, fluid can leak into the center of the macula, causing the macula to swell, resulting in blurred vision. This is known as diabetic macular edema. Macular edema can occur at any stage of diabetic retinopathy. Intravitreal VEGF injections have shown efficacy in treating DME and in preventing progression of diabetic retinopathy
- D. **Rare ocular conditions:** Conditions such as neovascular glaucoma, non-myopic causes of choroidal neovascularization, radiation retinopathy, and retinopathy of prematurity have historically been treated with bevacizumab. In 2023, Eylea became the first VEGF inhibitor to be FDA approved for retinopathy of prematurity.

Intraocular injections pose a risk for infection, retinal detachment, and traumatic lens injury. These injections require the treating physician to adhere to appropriate aseptic technique, educate individuals regarding

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

worrisome symptoms and monitor individuals after each injection as increases in intraocular pressure have been seen.

Biosimilar Agents: Biosimilar products must be highly similar to the reference product and there must be no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product. Biosimilars must utilize the same mechanism of action (MOA), route of administration, dosage form and strength as the reference product; and the indications proposed must have been previously approved for the reference product. The potential exists for a biosimilar product to be approved for one or more indications for which the reference product is licensed based on extrapolation of data intended to demonstrate biosimilarity in one indication. Sufficient scientific justification for extrapolating data is necessary for FDA approval. Factors and issues that should be considered for extrapolation include the MOA for each indication, the pharmacokinetics, bio-distribution, and immunogenicity of the product in different patient populations, and differences in expected toxicities in each indication and patient population.

- Bevacizumab biosimilars: Alymsys (bevacizumab-maly), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr) and Vegzelma (bevacizumab-adcd) are FDA approved biosimilar agents to Avastin. They share the same FDA approved uses as Avastin, with the exception of hepatocellular carcinoma. Alymsys, Mvasi, Zirabev and Vegzelma have not been studied in ophthalmic indications. However, since they have demonstrated biosimilarity to Avastin for FDA indications, biosimilarity may be extrapolated to other FDA indications and off-label indications, as well.
- Lucentis biosimilars: Byooviz (ranibizumab-nuna) is an FDA approved biosimilar to Lucentis and carries indications for AMD, retinal vein occlusion, and myopic choroidal neovascularization. The FDA approval of Byooviz was based on the totality of evidence demonstrating biosimilarity, including a randomized, double-masked, parallel group, multicenter phase 3 study in 705 patients with wet AMD. Results showed that after 24 weeks of monthly treatment with either Lucentis or Byooviz, the least square mean change in best corrected visual acuity (BCVA) from baseline to week 8 were 6.2 and 7.2 letters, respectively. The adjusted treatment difference between groups was -0.8 letters (90% CI, -1.8 to 0.2 letter), which was within the predefined equivalence limits of -3 to 3 letters. While Byooviz is not FDA approved for diabetic macular edema or diabetic retinopathy, efficacy may be extrapolated based on biosimilarity. Cimerli is designated as an interchangeable product (IP) to the reference product (RP) Lucentis. An Interchangeable product is approved based on data demonstrating that it is highly similar to an FDA-approved RP, that there are no clinically meaningful differences between the products. Per the FDA, interchangeable products can be expected to produce the same clinical result as the reference product (RP) in any given patient; and if administered more than once to a patient, the risk in terms of safety or diminished efficacy from alternating or switching between use of the RP and IP is not greater than that from the RP without such alternation or switch.
- Eylea biosimilars: Biosimilars are biological products that are highly similar to an existing FDA-approved reference product, with no clinically meaningful differences in terms of safety, purity, and potency. These products undergo a rigorous FDA approval process to ensure they meet the same high standards as the original reference product. Biosimilars offer comparable efficacy and safety, expanding treatment options while potentially reducing healthcare costs.
An interchangeable biosimilar is a specific type of biosimilar that satisfies additional regulatory criteria,

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

enabling it to be substituted for the reference product without the need for prescriber authorization. This substitution can take place at the pharmacy level, depending on state-specific pharmacy substitution laws. To obtain an interchangeable designation, manufacturers must provide additional data and studies that meet the FDA's stringent requirements, ensuring the product's safety and efficacy in repeated switching scenarios. Currently, there are five biosimilars to Eylea available on the market. Two of these, Yesafili (aflibercept-jbvf) and Opuviz (aflibercept-yszy), were approved as interchangeable biosimilars. The remaining three biosimilars, Ahzantive (aflibercept-mrbb), Pavblu (aflibercept-ayyh), and Enzeevu (aflibercept-abzv) were approved as non-interchangeable biosimilars.

* **Macugen** (pegaptanib) was discontinued by the manufacturer. Criteria will remain active until this drug has been removed from the drug file as claims can adjudicate several years after agent discontinuation.

Approved Indications

1. **Avastin (bevacizumab) and biosimilars:** Alymsys (bevacizumab-maly); Mvasi (bevacizumab-awwb); Vegzelma (bevacizumab-adcd); Zirabev (bevacizumab-bvzr)
 - A. Avastin has an off-label use to treat age-related macular degeneration (AMD).
2. **Beovu** (Brolucizumab-dbli)
 - A. Beovu is indicated for the treatment of Neovascular (Wet) Age-Related Macular Degeneration (AMD) and Diabetic Macular Edema (DME).
3. **Eylea** (Aflibercept) and biosimilars **Yesafili** (aflibercept-jbvf), **Opuviz** (aflibercept-yszy), **Ahzantive** (aflibercept-mrbb), **Pavblu** (aflibercept-ayyh), and **Enzeevu** (aflibercept-abzv):
 - A. Eylea is indicated for the treatment of Neovascular (Wet) Age-Related Macular Degeneration (AMD), Macular Edema Following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), Diabetic Retinopathy (DR) and Retinopathy of Prematurity (ROP).
4. **Lucentis** (Ranibizumab) and biosimilars: Byooviz (ranibizumab-nuna); Cimerli (ranibizumab-cqrn)
 - A. Lucentis is indicated for the treatment of Neovascular (Wet) Age-Related Macular Degeneration (AMD), Macular Edema Following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), Diabetic Retinopathy (DR) and Myopic Choroidal Neovascularization (mCNV).
5. **Vabysmo** (Faricimab-svoa)
 - i. Vabysmo is indicated for the treatment of Neovascular (Wet) Age-Related Macular Degeneration (nAMD), Diabetic Macular Edema (DME), and Macular Edema Following Retinal Vein Occlusion (RVO).
6. **Susvimo** (Ranibizumab)
 - A. Susvimo is indicated for the treatment of patients with Neovascular (wet) Age-related Macular Degeneration (AMD) who have previously responded to at least two intravitreal injections of a VEGF inhibitor.

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

Intravitreal injections of bevacizumab [Avastin] [Mvasi] [Zirabev] [Alymsys] [Vegzelma]

HCPCS	Description
C9257	Injection, bevacizumab, 0.25 mg [Avastin]
J9035	Injection, bevacizumab, 10 mg [when specified as Avastin intravitreal]
Q5126	Injection, bevacizumab-maly, biosimilar, 10 mg [Alymsys]
Q5129	Injection, bevacizumab-adcd, biosimilar, 10 mg [Vegzelma]
Q5107	Injection, bevacizumab-awwb, biosimilar, 10 mg [Mvasi]
Q5118	Injection, bevacizumab-bvzr, biosimilar, 10 mg [Zirabev]

ICD-10	Description
B39.0-B39.9	Histoplasmosis
E08.311-E08.3519	Diabetes mellitus due to underlying condition with diabetic retinopathy with macular edema [includes only codes E08.311 and ranges E08.3211-E08.3219, E08.3311-E08.3319, E08.3411-E08.3419, E08.3511-E08.3519, and E08.319 when specified as proliferative diabetic retinopathy]
E08.3521-E08.3599	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy [without macular edema]
E09.311-E09.3519	Drug or chemical induced diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E09.311 and ranges E09.3211-E09.3219, E09.3311-E09.3319, E09.3411-E09.3419, E09.3511-E09.3519, and E09.319 when specified as proliferative diabetic retinopathy]
E09.3521-E09.3599	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
E10.311-E10.3519	Type 1 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E10.311 and ranges E10.3211-E10.3219, E10.3311-E10.3319, E10.3411-E10.3419, E10.3511-E10.3519, and E10.319 when specified as proliferative diabetic retinopathy]
E10.3521-E10.3599	Type 1 diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
E11.311-E11.3519	Type 2 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E11.311 and ranges E11.3211-E11.3219, E11.3311-E11.3319, E11.3411-E11.3419, E11.3511-E11.3519, and E11.319 when specified as proliferative diabetic

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

	retinopathy]
E11.3521-E11.3599	Type 2 diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
E13.311-E13.3519	Other specified diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E13.311 and ranges E13.3211-E13.3219, E13.3311-E13.3319, E13.3411-E13.3419, E13.3511-E13.3519, and E13.319 when specified as proliferative diabetic retinopathy]
E13.3521-E13.3599	Other specified diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
H21.1X1-H21.1X9	Other vascular disorders of iris and ciliary body (neovascularization)
H30.001-H30.049	Focal chorioretinal inflammation
H30.101-H30.149	Disseminated chorioretinal inflammation
H30.891-H30.899	Other chorioretinal inflammations
H30.90-H30.93	Unspecified chorioretinal inflammation
H32	Chorioretinal disorders in diseases classified elsewhere
H34.8110	Central retinal vein occlusion, right eye, with macular edema
H34.8120	Central retinal vein occlusion, left eye, with macular edema
H34.8130	Central retinal vein occlusion, bilateral, with macular edema
H34.8190	Central retinal vein occlusion, unspecified eye, with macular edema
H34.8310	Tributary (branch) retinal vein occlusion, right eye, with macular edema
H34.8320	Tributary (branch) retinal vein occlusion, left eye, with macular edema
H34.8330	Tributary (branch) retinal vein occlusion, bilateral, with macular edema
H34.8330	Tributary (branch) retinal vein occlusion, bilateral, with macular edema
H34.8330	Tributary (branch) retinal vein occlusion, bilateral, with macular edema
H34.8330	Tributary (branch) retinal vein occlusion, bilateral, with macular edema
H34.8330	Tributary (branch) retinal vein occlusion, bilateral, with macular edema
H34.8390	Tributary (branch) retinal vein occlusion, unspecified eye, with macular edema
H35.00-H35.09	Background retinopathy and retinal vascular changes
H35.101-H35.179	Retinopathy of prematurity
H35.3210-H35.3293	Exudative age-related macular degeneration
H35.33	Angioid streaks of macula
H35.50-H35.54	H35.50-H35.54 Hereditary retinal dystrophy
H35.9	H35.9 Unspecified retinal disorder [specified as radiation retinopathy]
H40.50X0-H40.53X4	Glaucoma secondary to other eye disorders [neovascular glaucoma]
H40.89 Other	Other specified glaucoma [neovascular glaucoma]
H44.20-H44.23	Degenerative myopia
H44.2A1-H44.2A9	Degenerative myopia with choroidal neovascularization
Q82.8	Other specified congenital malformations of skin [pseudoxanthoma elasticum]
T66.XXXA-	Radiation sickness, unspecified [specified as radiation retinopathy]

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

T66.XXS

Intravitreal injections of ranibizumab [Lucentis] [Byooviz] [Cimerli]

HCPCS	Description
J2778	Injection, ranibizumab; 0.1 mg [Lucentis]
Q5124	Injection, ranibizumab-nuna, biosimilar, 0.1 mg (ranibizumab-nuna) [Byooviz]
Q5128	Injection, ranibizumab-eqrn biosimilar, 0.1 mg [Cimerli]

ICD-10	Description
E08.311-E08.3519	Diabetes mellitus due to underlying condition with diabetic retinopathy with macular edema [includes only codes E08.311 and ranges E08.3211-E08.3219, E08.3311-E08.3319, E08.3411-E08.3419, E08.3511-E08.3519, and E08.319 when specified as proliferative diabetic retinopathy]
E08.3521-E08.3599	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy [without macular edema]
E09.311-E09.3519	Drug or chemical induced diabetes mellitus with diabetic retinopathy with macular edema [includes only codes]
E09.3521-E09.3599	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
E10.311-E10.3519	Type 1 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E10.311 and]
E10.3521-E10.3599	Type 1 diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
E13.311-E13.3519	Other specified diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E13.311 and ranges E13.3211-E13.3219, E13.3311-E13.3319, E13.3411-E13.3419, E13.3511-E13.3519, and E13.319 when specified as proliferative diabetic retinopathy]
E13.3521-E13.3599	Other specified diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
H34.8120	Central retinal vein occlusion, left eye, with macular edema
H34.8110	Central retinal vein occlusion, right eye, with macular edema
H34.8120	Central retinal vein occlusion, left eye, with macular edema
H34.8130	Central retinal vein occlusion, bilateral, with macular edema
H34.8190	Central retinal vein occlusion, unspecified eye, with macular edema
H34.8310	Tributary (branch) retinal vein occlusion, right eye, with macular edema
H34.8320	Tributary (branch) retinal vein occlusion, left eye, with macular edema
H34.8330	Tributary (branch) retinal vein occlusion, bilateral, with macular edema
H34.8390	Tributary (branch) retinal vein occlusion, unspecified eye, with macular edema
H35.3210-H35.3293	Exudative age-related macular degeneration

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

H35.9	Unspecified retinal disorder [specified as radiation retinopathy]
H44.20-H44.23	Degenerative myopia
H44.2A1-H44.2A9	Degenerative myopia with choroidal neovascularization
T66.XXXA-T66.XXXS	Radiation sickness, unspecified [specified as radiation retinopathy]

Intravitreal injections of aflibercept [Eylea], aflibercept [Eylea HD], Yesafili (aflibercept-jbvf), Opuviz (aflibercept-yszy), Ahzantive (aflibercept-mrbb), Pavblu (aflibercept-ayyh), and Enzeevu (aflibercept-abzv)

HCPCS	Description
J0178	Injection, aflibercept, 1 mg [Eylea]
J0177	Injection, aflibercept hd, 1 mg [Eylea HD]
Q5147	Injection, aflibercept-ayyh (Pavblu), biosimilar, 1 mg
Q5149	Injection, aflibercept-abzv (Enzeevu), biosimilar, 1 mg
Q5150	Injection, aflibercept-mrbb (Ahzantive), biosimilar, 1 mg
Q5153	Injection, aflibercept-yszy (Opuviz), biosimilar, 1 mg
J3590	Unclassified biologics [when specified as Yesafili (aflibercept-jbvf)]
C9399	Unclassified drugs or biologics [when specified as Yesafili (aflibercept-jbvf)]

ICD-10	Description
E08.311-E08.3519	E08.311-E08.3519 Diabetes mellitus due to underlying condition with diabetic retinopathy with macular edema [includes only codes E08.311 and ranges E08.3211-E08.3219, E08.3311-E08.3319, E08.3411-E08.3419, E08.3511-E08.3519, and E08.319 when specified as proliferative diabetic retinopathy]
E08.3521-E08.3599	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy [without macular edema]
E10.311-E10.3519	Type 1 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E10.311 and ranges E10.3211-E10.3219, E10.3311-E10.3319, E10.3411-E10.3419, E10.3511-E10.3519, and E10.319 when specified as proliferative diabetic retinopathy]
E10.3521-E10.3599	Type 1 diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
E11.311-E11.3519	Type 2 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E11.311 and ranges E11.3211-E11.3219, E11.3311-E11.3319, E11.3411-E11.3419, E11.3511-E11.3519, and E11.319 when specified as proliferative diabetic retinopathy]
E11.3521-E11.3599	Type 2 diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
E13.311-E13.3519	Other specified diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E13.311 and ranges E13.3211-E13.3219, E13.3311-E13.3319, E13.3411-E13.3419, E13.3511-E13.3519, and E13.319 when specified as proliferative diabetic retinopathy]

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

E13.3521-E13.3599	Other specified diabetes mellitus with proliferative diabetic retinopathy [without macular edema]
H34.8110	Central retinal vein occlusion, right eye, with macular edema
H34.8120	Central retinal vein occlusion, left eye, with macular edema
H34.8130	Central retinal vein occlusion, bilateral, with macular edema
H34.8190	Central retinal vein occlusion, unspecified eye, with macular edema
H34.8310	Tributary (branch) retinal vein occlusion, right eye, with macular edema
H34.8320	Tributary (branch) retinal vein occlusion, left eye, with macular edema
H34.8330	Tributary (branch) retinal vein occlusion, bilateral, with macular edema
H34.8390	Tributary (branch) retinal vein occlusion, unspecified eye, with macular edema
H35.101-H35.169	Retinopathy of prematurity
H35.3210-H35.3293	Exudative age-related macular degeneration
H35.9	Unspecified retinal disorder [specified as radiation retinopathy]

Intravitreal injections of (brolucizumab-dbl) [Beovu]

HCPSC	Description
J0179	Injection, brolucizumab-dbl, 1 mg [Beovu]

ICD-10	Description
H35.3210-H35.3293	Exudative age-related macular degeneration
E08.311-E08.3519	Diabetes mellitus due to underlying condition with diabetic retinopathy with macular edema [includes only codes E08.311 and ranges E08.3211-E08.3219, E08.3311-E08.3319, E08.3411-E08.3419, E08.3511-E08.3519, when specified as proliferative diabetic retinopathy]
E09.311	Drug- or chemical-induced diabetes mellitus with unspecified diabetic retinopathy with macular edema
E09.3211-E09.3219	Drug or chemical-induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema.
E09.3311-E09.3319	Drug or chemical-induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E09.3411-E09.3419	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E09.3511-E09.3519	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema
E10.311-E10.3519	Type 1 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E10.311 and ranges E10.3211-E10.3219, E10.3311-E10.3319, E10.3411-E10.3419, E10.3511-E10.3519, when specified as proliferative diabetic retinopathy]
E11.311-E11.3519	Type 2 diabetes mellitus with diabetic retinopathy with macular edema [includes only

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

	codes E11.311 and ranges E11.3211-E11.3219, E11.3311-E11.3319, E11.3411-E11.3419, E11.3511-E11.3519, when specified as proliferative diabetic retinopathy]
E13.311-E13.3519	Other specified diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E13.311 and ranges E13.3211-E13.3219, E13.3311-E13.3319, E13.3411-E13.3419, E13.3511-E13.3519, when specified as proliferative diabetic retinopathy]

Intravitreal injections of Vabysmo (faricimab-svoa)

HCPCS	Description
J2777	Injection, faricimab-svoa, 0.1 mg [Vabysmo] (faricimab-svoa))

ICD-10	Description
H35.3210-H35.3293	Exudative age-related macular degeneration
E08.311-E08.3519	Diabetes mellitus due to underlying condition with diabetic retinopathy with macular edema [includes only codes E08.311 and ranges E08.3211-E08.3219, E08.3311-E08.3319, E08.3411-E08.3419, E08.3511-E08.3519, when specified as proliferative diabetic retinopathy]
E09.311	Drug- or chemical-induced diabetes mellitus with unspecified diabetic retinopathy with macular edema
E09.3211-E09.3219	Drug or chemical-induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema.
E09.3311-E09.3319	Drug or chemical-induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E09.3411-E09.3419	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E09.3511-E09.3519	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema
E10.311-E10.3519	Type 1 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E10.311 and ranges E10.3211-E10.3219, E10.3311-E10.3319, E10.3411-E10.3419, E10.3511-E10.3519, when specified as proliferative diabetic retinopathy]
E11.311-E11.3519	Type 2 diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E11.311 and ranges E11.3211-E11.3219, E11.3311-E11.3319, E11.3411-E11.3419, E11.3511-E11.3519, when specified as proliferative diabetic retinopathy]
E13.311-E13.3519	Other specified diabetes mellitus with diabetic retinopathy with macular edema [includes only codes E13.311 and ranges E13.3211-E13.3219, E13.3311-E13.3319, E13.3411-E13.3419, E13.3511-E13.3519, when specified as proliferative diabetic retinopathy]

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

A. Criteria For Initial Approval

1. Vabysmo (faricimab-svoa)

Requests for Vabysmo (faricimab-svoa) may be approved if the following criteria are met:

- I. Individual has a diagnosis of one of the following:
 - A. Established neovascular "wet" age-related macular degeneration; **OR**
 - B. Diabetic macular edema (DME) (including DME with diabetic retinopathy of any severity); **OR**
 - C. Macular Edema following Retinal Vein Occlusion (RVO)

Requests for Vabysmo (faricimab-svoa) may not be approved when the above criteria are not met and for all other indications.

2. Avastin (bevacizumab); Alymsys (bevacizumab-maly); Mvasi (bevacizumab-awwb); Vegzelma (bevacizumab-adcd); Zirabev (bevacizumab-bvzr)

Requests for Avastin (bevacizumab), Alymsys (bevacizumab-maly), Mvasi (bevacizumab-awwb), Vegzelma (bevacizumab-adcd), or Zirabev (bevacizumab-bvzr) may be approved if the following criteria are met:

- I. Individual has a diagnosis of one of the following:
 - A. Diabetic macular edema (including DME with diabetic retinopathy of any severity) (AAO 2019); **OR**
 - B. Proliferative or moderate to severe non-proliferative diabetic retinopathy with or without diabetic macular edema (AAO2019, DP B IIa); **OR**
 - C. Established neovascular "wet" age-related macular degeneration (AHFS); **OR**
 - D. Macular edema from branch retinal vein occlusion (AAO 2019); **OR**
 - E. Macular edema from central retinal vein occlusion (AAO 2019); **OR**
 - F. Neovascular glaucoma (Costagliola 2008, DP B IIb); **OR**
 - G. Choroidal neovascularization associated with myopic degeneration (AAO Consensus 2017, DP B IIb); **OR**

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

- H. Other rare causes of choroidal neovascularization for one or more of the following conditions (Weber 2016):
 - 1.angioid streaks; **OR**
 - 2.choroiditis (including, but not limited to histoplasmosis induced choroiditis); **OR**
 - 3.retinal dystrophies; **OR**
 - 4.trauma; **OR**
 - 5.pseudoxanthoma elasticum; **OR**
- I. Radiation retinopathy (Finger 2016); **OR**
- J. Retinopathy of prematurity (Sankar 2018, DP B IIb).

Requests for intravitreal injections of Avastin (bevacizumab), Alymsys (bevacizumab-maly), Mvasi (bevacizumab-awwb), Vegzelma (bevacizumab-adcd), or Zirabev (bevacizumab-bvzr) may not be approved when the above criteria are not met and for all other indications.

3. Lucentis (ranibizumab); Byooviz (ranibizumab-nuna); Cimerli (ranibizumab-cqrn)

Requests for Lucentis (ranibizumab), Byooviz (ranibizumab-nuna), or Cimerli (ranibizumab-cqrn) may be approved if the following criteria are met:

- I. Individual has a diagnosis of one of the following:
 - A. Diabetic macular edema (including DME with diabetic retinopathy of any severity);**OR**
 - B. Diabetic Retinopathy (DR); **OR**
 - C. Established neovascular “wet” Age-related Macular Degeneration (AMD); **OR**
 - D. Macular edema following Retinal Vein Occlusion (RVO); **OR**
 - E. Myopic Choroidal Neovascularization (mCNV); **OR**
 - F. Radiation retinopathy (Finger 2016)

Requests for intravitreal injections Lucentis (ranibizumab), Byooviz (ranibizumab-nuna), or Cimerli (ranibizumab-cqrn) may not be approved when the above criteria are not met and for all other indications.

4. Eylea (aflibercept) and biosimilars Yesafili (aflibercept-jbvf), Opuviz (aflibercept-yszy), Ahzantive (aflibercept-mrbb), Pavblu (aflibercept-ayyh), and Enzeevu (aflibercept-abzv)

- I. Requests for Eylea (aflibercept) and biosimilars may be approved if the following criteria are met:
 - A. Diabetic macular edema (including DME with diabetic retinopathy of any severity); **OR**
 - B. Diabetic Retinopathy (DR); **OR**
 - C. Established neovascular “wet” age-related macular degeneration; **OR**
 - D. Macular edema following Retinal Vein Occlusion (RVO); **OR**
 - E. Retinopathy of prematurity.

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

Requests for intravitreal injections of Eylea (aflibercept) and biosimilars may not be approved when the above criteria are not met and for all other indications.

5. Eylea HD (aflibercept)

a. Requests for Eylea HD (aflibercept) may be approved if the following criteria are met:

- i. Individual has a diagnosis of one of the following:
 1. Neovascular (wet) age-related macular degeneration (nAMD); **OR**
 2. Diabetic retinopathy (DR); **OR**
 3. Diabetic macular edema (DME).

Requests for intravitreal injections of Eylea HD (aflibercept) may not be approved when the above criteria are not met and for all other indications.

6. Beovu (brolucizumab-dblI)

Requests for Beovu (brolucizumab-dblI) may be approved if the following criteria are met:

- I. Individual has a diagnosis of one of the following:
 - A. Established neovascular “wet” age-related macular degeneration (AMD); **OR**
 - B. Diabetic macular edema (including DME with diabetic retinopathy of any severity)

Requests for intravitreal injections of Beovu (brolucizumab-dblI) may not be approved when the above criteria are not met and for all other indications.

7. Susvimo (Ranibizumab)

Requests for Susvimo (Ranibizumab) may be approved if the following criteria are met:

- A. Diagnosis of neovascular “wet” age-related macular degeneration (AMD); **AND**
- B. Documented evidence that the patient has previously responded to at least two intravitreal injections of a VEGF inhibitor.

Requests for intravitreal injections of Susvimo (Ranibizumab) may not be approved when the above criteria are not met and for all other indications.

B. Criteria for Continuation of Therapy

- i. MMM considers continuation of VEGF inhibitors therapy medically necessary in members requesting reauthorization when the maximum duration of therapy has not been exceeded, and the following information is provided for reauthorization:
 - a. Documented evidence that the patient has responded to treatment; **AND**
 - b. Documentation that additional doses are clinically necessary; **AND**
 - c. Prescribed dosage follows FDA approved labeling (see the drug PI for additional

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

information)

- ii. When Vabysmo is used to treat Macular Edema following Retinal Vein Occlusion (RVO), the maximum duration of therapy as recommended by the manufacturer is 6 months.

C. Authorization Duration

- i. Initial Approval Duration: Up to 12 months
 - 1. Vabysmo initial approval duration when used for Macular Edema following Retinal Vein Occlusion (RVO): 6 months
 - 2. Lucentis and biosimilars initial approval duration when used for Myopic Choroidal Neovascularization: 3 months
- ii. Reauthorization Approval Duration: Up to 12 months
 - 1. Patients may receive additional courses of Lucentis or biosimilars (up to three months of treatment) for Myopic Choroidal Neovascularization

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

Requests for VEGF inhibitors may not be approved when the above criteria (Section A: Criteria for Initial Approval) are not met and for all other indications.

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

Limits or Restrictions

A. Step Therapy

This medical policy may be subject to Step Therapy. Please refer to the document published on the MMM Website: <https://www.mmm-pr.com/planes-medicos/formulario-medicamentos>

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

• Drug	Indication & Dosage
Eylea (aflibercept) 2 mg vial Yesafili (aflibercept-jbvf) 2 mg vial Opuviz (aflibercept-yszy) 2 mg vial AHzantive (aflibercept-mrbb) 2 mg vial Pavblu (aflibercept-ayyh) 2 mg vial and Enzeevu (aflibercept-abzv) 2 mg vial	• Diabetic macular edema, diabetic retinopathy, neovascular “wet” age- related macular degeneration, retinal vein occlusion: 2 mg per eye; each eye may be treated as frequently as every 4 weeks • Retinopathy of prematurity: 0.4 mg per eye; each eye may be treated as frequently as every 10 days
Eylea HD (aflibercept) 8 mg vial	• Neovascular (wet) age-related macular degeneration, Diabetic Macular Edema (DME), Diabetic Retinopathy (DR): 8 mg per eye every 4 weeks for the first three doses; followed by 8 mg per eye; each eye may be treated as frequently as every 8 weeks.
Lucentis (ranibizumab); Cimerli (ranibizumab-eqrn)	• Diabetic macular edema and diabetic retinopathy: 0.3 mg per eye; each eye may be treated as frequently as every 4 weeks • Age related macular degeneration, branch or central retinal vein occlusion, myopic choroidal neovascularization, and radiation retinopathy: 0.5 mg per eye; each eye may be treated as frequently as every 4 weeks
Byooviz (ranibizumab-nuna)	0.5 mg per eye; each eye may be treated as frequently as every 4 weeks
Avastin (bevacizumab); Alymsys (bevacizumab-maly); Mvasi (bevacizumab-awwb);	1.25 mg per eye; each eye may be treated as frequently as every 4 weeks

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

Vegzelma (bevacizumab-adcd); Zirabev (bevacizumab-bvzr)	
Beovu (brolucizumab-dbli)	6 mg per eye; each eye may be treated as frequently as every 8 weeks**
Vabysmo (faricimab-svoa)	6 mg per eye; each eye may be treated as frequently as every 4 weeks
Susvimo (ranibizumab)	2-mg every 24 weeks. Supplemental treatment with 0.5 mg intravitreal ranibizumab injection may be administered in the affected eye if clinically necessary.
Exceptions	
**For Beovu, may approve the following for initiation of therapy: I. Age-related macular degeneration: One 6 mg dose per eye monthly for the first three (3) doses;OR II. Diabetic macular edema (DME): One 6 mg dose per eye every six weeks for the first five (5) doses.	

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

Reference Information

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Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.

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Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Select Review 8/25/2025	Addition of clinical criteria for Eylea HD. Coding review for Eylea and Biosimilars: Added HCPCS Q5147 for Pavblu, Q5149 for Enzeevu, and Q5150 for Ahzantive effective 4/1/25. For Opuviz added Q5153 effective 7/1/25.	9/5/2025	9/16/2025
Select Review	Add new biosimilars Yesafili, Opuviz, Ahzantive, Pavblu, Enzeevu to Eylea's clinical criteria and quantity limits. Coding Reviewed: Added HCPCS J3590 [when specified as Yesalfi, Opuviz, Ahzantive, Pavblu, Enzeevu]. Add that Lucentis and biosimilars, when used for Myopic Choroidal Neovascularization, the initial approval will be for 3 months and courses can be repeated if clinically necessary.	11/18/2024	12/17/2024
Annual Review	Updated Vabysmo criteria to include the FDA label expansion to include Macular Edema following retinal vein occlusion. Added quantity limits to Vabysmo for this indication. Removed obsolete agent, Macugen. Coding Reviewed: Deleted CPT 67028, HCPCS J2503, and ICD-10-CM H35.3210-H35.3293 for Macugen. Effective 1/1/2024 Added HCPCS C9161 for Eyelea HD. Effective 4/1/2024 Added HCPCS J0177 for Eylea HD. Removed HCPCS J3490, J3590, C9161.	3/25/2024	6/28/2024
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Vascular Endothelial Growth Factor (VEGF) Inhibitors	MP-RX-FP-100-23	☒ MMM MA ☒ MMM Multihealth